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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	Applicati n Numb r	09/163272	
	Filing Date	September 29, 1998	
	First Named Inventor	Jonathan Dinsmore	
	Group Art Unit	1632	
	Examiner Name	Anne Baker	
Total Number of Pages in This Submission	108	Attorney Docket Number	DNI-041CPA

ENCLOSURES (check all that apply)		
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#28  
BP  
2-12-03

In re the application f: Jonathon Dinsmore

Serial No.: 09/163,272

Filed: September 29, 1998

(CPA filed on May 3, 2002)

For: *Porcine Spinal Cord Cells and Their  
Use in Spinal Cord Repair*

Attorney Docket No.: DNI-041CPA

Group Art Unit: 1632

Examiner: Anne-Marie Baker,  
Ph.D.



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January 16, 2003  
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By:

Megan E. Williams, Esq.  
Reg. No. 43,270  
Attorney for Applicants

RESPONSE TO OFFICE ACTION

Dear Sir:

In response to the Office Action dated July 16, 2002 (Paper No. 25), Applicants submit the following remarks. A request for the appropriate extension of time in which to respond is being filed concurrently herewith. For the Examiner's convenience, a list of the currently pending claims is attached herewith as Appendix A. Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of the claims under 35 U.S.C. § 103(a).

Rejection of 1, 3-8, 10-18, 20-26, and 28-48 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1, 3-8, 10-18, 20-26, and 28-48 under 35 U.S.C. §112, first paragraph. The Examiner states that while the specification, "is enabling for a method of treating a xenogeneic subject having spinal cord damage arising from amyotrophic lateral sclerosis," the specification, "does not reasonably provide enablement for treating a xenogeneic subject having spinal cord damage arising from the claim-designated neurodegenerative disorders, spinal cord injuries, or aging." This rejection is respectfully traversed.

The pending claims are directed to a composition for transplantation into a mammalian xenogeneic subject comprising isolated spinal cord cells obtained from an embryonic pig of between about 24 and about 35 days of gestation, such that treatment of spinal cord damage that would benefit from survival and integration of the spinal cord cells is obtained upon transplantation into the subject. The pending claims are also directed to a method of treating a mammalian xenogeneic subject having spinal cord damage that would benefit from survival and integration of porcine spinal cord cells by administering to the subject a composition comprising isolated spinal cord cells obtained from an embryonic pig of between about 24 and about 35 days of gestation, such that treatment of spinal cord damage is obtained upon administration of the composition to the subject.

Applicants maintain that the instant specification fully enables one of ordinary skill in the art to treat spinal cord damage as claimed. Applicants provide working examples in the specification of successful transplantations using embryonic porcine spinal cord cells. Specifically, as described in Example III, Applicants provide results from successful transplantation of porcine spinal cells into SOD mice, which is a mouse model for ALS. In Example II, Applicants also provide results from successful transplantation of porcine spinal cells into hemi-sected rats, *which serves as a model for spinal cord injury*. Applicants maintain that these examples and the indications related

to the animal models which are used, should not be used to limit the claimed invention as suggested by the Examiner.

In addition to the evidence provided in the specification that spinal cord damage, including damage resulting from neurodegenerative disorders, spinal cord injuries, and aging, can be treated using the claimed methods, Applicants provide herewith a Declaration Under 37 C.F.R. § 1.132 of Dr. Jonathan Dinsmore (hereinafter referred to as "The Dinsmore Declaration").

The Dinsmore Declaration contains results which clearly demonstrate that the specification of the instant invention enables one of ordinary skill in the art to use the claimed compositions and methods for treatment of spinal cord damage in general, not just for treatment of ALS. The Dinsmore Declaration contains data obtained in Phase I clinical trials approved by the FDA. The data shown in the Dinsmore Declaration demonstrate that transplantation of embryonic porcine spinal cord cells into human subjects having various types of spinal cord damage can improve both the motor and sensory function of the subjects. The types of spinal cord damage shown to be improved by transplantation of embryonic porcine spinal cord cells include spinal cord injury resulting from trauma to both the upper (cervical) and lower (lumbar) regions of the spinal cord and transverse myelitis (TM), a neurodegenerative disorder. Results shown in Appendix E of the Dinsmore Declaration were obtained from transplant recipients who were regularly examined for improvements in their overall impairment. Each recipient showed improvement in the months following transplantation of embryonic porcine spinal cord cells, including improvements in motor and sensory functions and impairment. Evaluations of the recipients were performed according to the standard established by the American Spinal Injury Association (ASIA).

Based on the ASIA rating system, impairment was rated on a scale of A-E, where the lowest rating (A) indicates complete impairment, *i.e.*, no motor or sensory function is preserved in the sacral segments, and the highest rating (E) indicates normal motor and

sensory function. Impairment improved in each recipient where impairment was evaluated. Recipient CLO-02, who had transverse myelitis, improved from an A rating to a C rating within a year of receiving transplanted porcine cells. Furthermore, recipients LDS-04 and SRL-05, who both had lumbar spinal cord injuries resulting from trauma, improved from an A rating to a B rating within the first five months of transplantation.

Motor skills were also assessed using the ASIA motor score rating system, wherein both the right and left side of the individual is examined and given a score of up to 50 for each side, with a total potential score of 100. As shown in Appendix E, each of the transplant recipients showed an increase in their motor score rating in the months following embryonic porcine cell transplantation. For example, for recipient WDS-03, who had a cervical spinal cord injury caused by trauma, the motor score rating increased in the months following the transplantation, rising from a score of 30 to 32 by the ninth month. In another example, recipient LDS-04, who had a lumbar spinal cord injury caused by trauma, had a baseline score of 52 at the time of the transplantation and increased the score to 54 in the two months following the transplantation.

Sensory skills were also assessed using the ASIA motor score rating system, wherein both the right and left side of the individual is examined using the pin prick test and the light touch test. Based on the subject's response to each test, the subject is given a score of up to 56 for each test on each side, with a total potential score of 224. As shown in Appendix E of the Dinsmore Declaration, each of the transplant recipients showed an increase in their sensory score rating in the months following embryonic porcine cell transplantation. For example recipient LDS-04 who had a lumbar spinal cord injury resulting from trauma showed an improved sensory score of 142 to 148 in the two months following the transplantation. In another example, recipient CLO-02 who had transverse myelitis showed an improved sensory score from 158 to 189 in the twelve months following the transplantation.

Accordingly, the data presented in the Dinsmore Declaration demonstrate that the transplantation of xenogeneic porcine spinal cord cells can be used effectively as treatment for improving both the sensory and motor function of human subjects having spinal cord damage.

The Examiner has cited Jackowski, *et al.* in support of the assertion that Applicants have not enabled the claimed invention because "methods of transplantation of neural tissue are not routinely successful" due to the unpredictability and limitations associated with the transplantation process. The Jackowski reference examines the potential for regeneration of nerves in damaged adult CNS. In contrast to the Examiner's assertion, Applicants submit that Jackowski does not teach that neural cell transplantation is unsuccessful, but rather teaches the benefits of using fetal cells for such transplantation. (Applicants note, however, that the reference does not teach Applicants' invention of transplanting spinal cord cells obtained from an embryonic pig of between about 24 and about 35 days of gestation, such that treatment of spinal cord damage that would benefit from survival and integration of the spinal cord cells is obtained upon transplantation into the subject). On page 311, second column, first paragraph, Jackowski states that, "Whilst regenerating CNS axons are strongly inhibited or halted in their regrowth by such influences, it appears that the initially formed growth cones of transplanted foetal CNS neurons, perhaps lacking in or not yet expressing the appropriately responsive receptors, are exempt from such inhibitory molecules." Jackowski later suggests again (in the following paragraph) that one possible avenue for promoting regeneration is "the use of microtransplanted embryonic donor cell suspensions, to recreate important innervating centres that have been lost or irreparably damaged." Thus, the reference does not teach that neural transplantation is routinely successful. Applicants respectfully submit that in view of the successful Phase I clinical transplantations described in the Dinsmore Declaration and the successful examples of xenogeneic transplantation described in the specification, one of ordinary skill in the art would be able to make and use the claimed

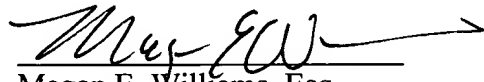
compositions and practice the claimed methods using no more than routine experimentation.

Applicants maintain that the specification provides ample support for use of porcine spinal cord cells for treatment of spinal cord damage as claimed, resulting from, e.g., spinal cord injuries or neurodegenerative disorders. Applicants respectfully submit that the teachings in the specification enable the treatment of a variety of different types of deficits that would benefit from transplantation of fetal spinal cord cells.

### CONCLUSION

It is respectfully submitted that this application is in condition for allowance. If the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,  
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